Claims

What we claim is:

1. A method for selecting a treatment for a patient suffering from a condition or disease, comprising

determining whether cells of said patient contain at least one variance of a gene, wherein the presence or the absence of said variance in said cells is indicative of the effectiveness of said treatment for said condition or disease,

wherein said gene is a folate transport or metabolism gene or a pyrimidine transport or metabolism gene.

2. The method of claim 1, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase.

3. The method of claim 1, wherein the presence of said at least one variance is indicative that said treatment will be effective for said patient.

4. The method of claim 1, wherein the presence of said variance is indicative that said treatment will be ineffective or contra-indicated for said patient.

5. The method of claim 1, wherein said at least one variance comprises a plurality of variances.

6. The method of claim 5, wherein said plurality of variances comprise a haplotype or haplotypes.

7. The method of claim 1, wherein said selecting a treatment further comprises identifying a compound differentially active on a form of said gene containing said at least one variance.

8. The method of claim 1, wherein said compound is selected from the group consisting of a reduced folate, a folate analog, folic acid, a fluoropyrimidine, a dihydropyrimidine dehydrogenase inhibitor, a cytidine analog, a pyrimidine analog, a ribonucletide reductase inhibitor, and a nucleotide/nucleoside uptake inhibitor.

9. The method of claim 1, wherein said selecting a treatment further comprises eliminating a treatment, wherein said presence or absence of said at least one variance is indicative that said treatment will be ineffective or contra-indicated.

10. The method of claim 1, wherein said treatment comprises a first treatment and a second treatment, said method comprising the steps of:

identifying a said first treatment effective to treat said disease or condition; and

identifying a said second treatment which reduces a deleterious effect of said first treatment.

11. The method of claim 1, wherein said selecting a treatment further comprises selecting the method of administration of a compound effective to treat said disease, wherein said presence or absence of said at least one variance is indicative of the appropriate method of administration for said compound.

12. The method of claim 11, wherein said selecting the method of administration comprises selecting a suitable dosage level or frequency of administration of a compound.

13. The method of claim 1, further comprising determining the level of expression of said gene or the level of activity of a protein containing a polypeptide expressed from said gene,

wherein the combination of the determination of the presence or absence of said at least one variance and the determination of the level of activty or the level of expression provides a further indication of the effectiveness of said treatment.

14. The method of claim 1, wherein said disease or condition is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida.

15. The method of claim 1, wherein the detection of the presence or absence of said at least one variance comprises amplifying a segment of nucleic acid including at least one of said variances.

16. The method of claim 15, wherein said segment of nucleic acid is 500 nucleotides or less in length.

17. The method of claim 15, wherein said segment of nucleic acid is 100 nucleotides or less in length.

18. The method of claim 15, wherein said segment of nucleic acid is 45 nucleotides or less in length.

19. The method of claim 15, wherein said segment includes a plurality of variances.

20. The method of claim 1, wherein the detection of the presence or absence of said at least one variance comprises contacting nucleic acid comprising a variance site with at least one nucleic acid probe, wherein said at least one probe preferentially hybridizes with a nucleic acid sequence including said variance site and containing a complementary base at said variance site under selective hybridization conditions.

21. The method of claim 1, wherein the detection of the presence or absence of said at least one variance comprises sequencing at least one nucleic acid sequence.

22. The method of claim 1, wherein the detection of the presence or absence of said at least one variance comprises mass spectrometric determination of at least one nucleic acid sequence.

23. The method of claim 1, wherein the detection of the presence or absence of said at least one variance comprises determining the haplotype of a plurality of variances in a gene.

24. A method for selecting a method of treatment, comprising

comparing at least one variance in at least one gene in a patient suffering from a disease or condition with a list of variances in said at least one gene indicative of the effectiveness of at least one method of treatment, wherein said at least one gene is a folate transport or metabolism gene or a pyrimidine transport or metabolism gene.

25. The method of claim 24, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase.

26. The method of claim 24, wherein said at least one variance comprises a plurality of variances.

27. The method of claim 24, wherein said list of variances comprises a plurality of variances.

28. The method of claim 24, wherein at least one said method of treatment comprises the administration of a compound effective against said disease or condition to a patient.

29. The method of claim 28, wherein said compound is selected from the group consisting of reduced folate, a folate analog, folic acid, a fluoropyrimidine, a dihydropyrimidine dehydrogenase inhibitor, a cytidine analog, a pyrimidine analog, a ribonucletide reductase inhibitor, and a nucleotide/nucleoside uptake inhibitor.

30. The method of claim 24, wherein the presence or absence of at least one variance in said gene is indicative that said treatment will be effective in said patient.

31. The method of claim 24, wherein the presence or absence of at least one variance in said gene is indicative that said treatment will be ineffective or contra-indicated.

32. The method of claim 24, wherein said treatment is a first treatment and the presence or absence of at least one variance in said gene is indicative that a second treatment will be beneficial to reduce a deleterious effect of said first treatment.

33. The method of claim 24, wherein said at least one method of treatment is a plurality of methods of treatment.

34. The method of claim 33, wherein said selecting comprises determining whether any of said plurality of methods of treatment will be more effective than at least one other of said plurality of methods of treatment.

35. The method of claim 24, wherein said disease is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida.

36. A method for selecting a method of administration to a patient suffering from a condition or disease for a compound or compounds effective to treat said condition or disease, comprising the step of

determining whether at least one variance in a gene is present or absent in cells of said patient, wherein said presence or absence of said at least one variance is indicative of an appropriate method of administration for said compound, and

wherein said gene is a folate transport or metabolism or pyridine transport or metabolism gene.

37. The method of claim 36, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase.

38. The method of claim 36, wherein said selecting a method of administration comprises selecting a dosage level or frequency or frequency of administration of said compound.

39. The method of claim 36, wherein said drug is selected from the group consisting of reduced folate, a folate analog, folic acid, a fluoropyrimidine, a dihydropyrimidine dehydrogenase inhibitor, a cytidine analog, a pyrimidine analog, a ribonucletide reductase inhibitor, and a nucleotide/nucleoside uptake inhibitor.

40. The method of claim 36, wherein said disease is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida .

41. A method for selecting a patient for administration of a method of treatment, comprising

comparing the presence or absence of at least one variance in a gene in cells of a patient suffering from a disease or condition with a list of variances in said gene, wherein the presence or absence of said at least one variance in said cells is indicative that said treatment will be effective in said patient; and

determining whether said patient will receive said method of treatment based on the presence or absence of said at least one variance in said cells,

wherein said gene is a folate transport or metabolism gene or a pyrimidine transport or metabolism gene.

42. The method of claim 41, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

43. The method of claim 41, wherein said method of treatment comprises administration of a compound effective against said disease or condition.

44. The method of claim 43, wherein said disease is selected from the group consisting of reduced folate, a folate analog, folic acid, a fluoropyrimidine, a dihydropyrimidine dehydrogenase inhibitor, a cytidine analog, a pyrimidine analog, a ribonucletide reductase inhibitor, and a nucleotide/nucleoside uptake inhibitor .

45. The method of claim 41, wherein said determining comprises assigning said patient to a group to receive said method of treatment or to a control group.

46. A method for identifying the presence or absence of at least one form of a gene in cells of an individual, comprising the steps of:

a) determining the presence or absence of at least one variance in said gene in said cells, wherein said gene is a folate transport or metabolism or pyrimidine transport or metabolism gene.

47. The method of claim 46, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

48. The method of claim 46, wherein said individual suffers from a disease or condition.

49. The method of claim 46, wherein the presence or absence of said at least one variance is indicative of the effectiveness of a therapeutic treatment in a patient having cells containing said at least one variance.

50. The method of claim 46, wherein said determining comprises amplifying a segment of nucleic acid including a site of at least one of said at least one variance.

51. The method of claim 46, wherein said determining comprises contacting a nucleic acid sequence containing a variance site corresponding to a said variance with a probe which specifically binds under selective binding conditions to a nucleic acid sequence comprising at least one said variance.

52. The method of claim 46, wherein the detection of the presence or absence of said at least one variance comprises sequencing at least one nucleic acid sequence.

53. The method of claim 46, wherein the detection of the presence or absence of said at least one variance comprises mass spectrometric determination of at least one nucleic acid sequence.

54. The method of claim 46, wherein the detection of the presence or absence of said at least one variance comprises determining the haplotype of a plurality of variances in a gene.

55. A pharmaceutical composition comprising

a compound which has a differential effect in patients having at least one copy of a particular form of a gene, wherein said gene is a folate transport or metabolism gene or a pyrimidine transport or metabolism gene; and

a pharmaceutically acceptable carrier or excipient or diluent,

wherein said composition is adapted to be preferentially effective to treat a patient with cells comprising a form of said gene comprising at least one variance.

56. The composition of claim 55, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-

drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

57. The compositon of claim 55, wherein said patient suffers from a disease or condition selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida .

58. The pharmaceutical composition of claim 55, wherein said pharmaceutical composition is subject to a regulatory limitation restricting the use of said pharmaceutical composition to patients having at least one copy of a form of a gene comprising at least one variance.

59. The pharmaceutical composition of claim 55, wherein said pharmaceutical composition is subject to a regulatory limitation indicating said pharmaceutical composition is not to be used in patients having at least one copy of a form of a gene comprising at least one variance.

60. The pharmaceutical composition of claim 55, wherein said pharmaceutical composition is packaged, and the packaging includes a label or insert restricting the use of said pharmaceutical composition to patients having at least one copy of a form of a gene comprising at least one variance.

61. The pharmaceutical composition of claim 55, wherein said pharmaceutical composition is packaged, and said packaging includes a label or insert requiring the use

of a test to determine the presence or absence of at least one variance in cells of a said patient.

62. A probe which specifically binds under selective binding conditions to a nucleic acid sequence comprising at least one variance in a gene selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

63. The probe of claim 62, wherein said probe comprises a nucleic acid sequence 500 nucleotide bases or fewer in length.

64. The probe of claim 62, wherein said nucleic acid sequence is 100 or fewer nucleotide bases in length.

65. The probe of claim 62, wherein said nucleic acid sequence is 25 or fewer nucleotide bases in length.

66. The probe of claim 62, wherein said probe comprises DNA.

67. The probe of claim 62, wherein said probe comprises DNA and at least one nucleic acid analog.

68 The probe of claim 62, wherein said probe comprises peptide nucleic acid (PNA

69. The probe of claim 62, further comprising a detectable label.

70. The probe of claim 69, wherein said detectable label is a fluorescent label.

71. A method for determining a genotype of an individual, comprising analyzing at least one nucleic acid sequence from cells of said individual using mass spectrometric analysis,

wherein said nucleic acid sequence is a portion of a folate transport or metabolism gene or pyrimidine transport or metabolism gene or a complementary sequence.

72. The method of claim 71, wherein said analyzing a nucleic acid sequence comprises determining the presence or absence of a variance in said gene.

73. The method of claim 71, wherein said analyzing a nucleic acid sequence comprises determining the nucleotide sequence of said at least one nucleic acid sequence.

74. The method of claim 71, wherein said at least one nucleic acid sequence is 500 nucleotides or less in length.

75. The method of claim 71, wherein said at least one nucleic acid sequence comprises at least one variance site in said gene.

76. An isolated, purified or enriched nucleic acid sequence of 15 to 500 nucleotides in length, comprising at least one variance, wherein said sequence has the base sequence of a portion of an allele of a gene selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate

synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase or a sequence complementary thereto.

77. The nucleic acid sequence of claim 76, wherein said nucleic acid sequence is 15 to 100 nucleotide bases in length.

78. The nucleic acid sequence of claim 76, wherein said nucleic acid sequence sequence is 15 to 25 nucleotide bases in length.

79. A method for determining whether a compound has differential effects on cells containing at least one different form of a folate transport or metabolism or pyridine transport or metabolism gene, comprising the steps of:

contacting a first cell and a second cell with said compound, wherein said first cell and said second cell differ in the presence or absence of at least one variance in said gene; and

determining whether the response of said first cell and said second cell to said compound differ, wherein the difference in said response is due to the presence or absence of said at least one variance.

80. The method of claim 79, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-

iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl-transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

81. The method of claim 79, wherein at least one of said first cell and said second cell are contacted *in vivo*.

82. The method of claim 79, wherein at least one of said first cell and said second cell are contacted *in vitro*.

83. The method of claim 81, wherein at least one of said first cell and said second cell is contacted *in vivo* in a plurality of patients suffering from a disease or condition

84. A method of treating a patient suffering from a condition or disease, comprising the steps of:

a) determining whether cells of said patient contain a form of a gene which comprises at least one variance, wherein the presence or absence of said at least one variance is indicative that a treatment will be effective in said patient; and

b) administering said treatment to said patient.

85. The method of claim 84, wherein said gene is a folate transport or metabolism gene or a pyrimidine transport or metabolism gene. .

86. The method of claim 84, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase,

Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formyltetrahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate formiminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

87. The method of claim 84, wherein said disease is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida .

88. The method of claim 84, wherein the presence of said at least one variance is indicative that said treatment will be effective in said patient.

89. The method of claim 88, wherein said treatment comprises the administration of a compound preferentially active for said condition or disease in a said patient having said at least one variance in said gene.

90. The method of claim 89, wherein said compound is selected from the group consisting of reduced folate, a folate analog, folic acid, a fluoropyrimidine, a dihydropyrimidine dehydrogenase inhibitor, a cytidine analog, a pyrimidine analog, a ribonucletide reductase inhibitor, and a nucleotide/nucleoside uptake inhibitor .

91. The method of claim 84, wherein the presence of said at least one variance in said gene is indicative of an appropriate dosage or frequency of administration of a compound in said treatment.

92. A method of treating a patient suffering from a disease or condition, comprising the steps of:

a) comparing the presence or absence of at least one variance in at least one gene in cells of a patient suffering from a disease or condition with a list of variances in said at least one gene indicative of the effectiveness of at least one method of treatment;

b) selecting a method of treatment from said at least one method of treatment, wherein the presence or absence of at least one of said at least one variance is indicative that said method of treatment will be effective in said patient; and

c) administering said method of treatment to said patient.

93. The method of claim 92, wherein said at least one gene comprises a folate transport or metabolism or pyrimidine transport or metabolism gene.

94. The method of claim 92, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

95. The method of claim 92, further comprising determining the presence or absence of said at least one variance in cells of said patient.

96. The method of claim 92, wherein said at least one variance comprises a plurality of variances.

97. The method of claim 92, wherein said list of variances comprises a plurality of variances.

98. The method of claim 97, wherein said plurality of variances comprises a haplotype or haplotypes.

99. The method of claim 92, wherein said method of treatment comprises the administration of a compound effective against said disease or condition.

100. The method of claim 92, wherein said treatment is a first treatment and the presence or absence of at least one variance in said gene is indicative that a second treatment will be beneficial to reduce a deleterious effect of said first treatment.

101. The method of claim 92, wherein said at least one method of treatment is a plurality of methods of treatment.

102. The method of claim 92, wherein said disease or condition is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida .

103. A method of treating a patient suffering from a disease or condition, comprising the steps of:

a) comparing the presence or absence of at least one variance in at least one gene in cells of a patient suffering from a disease or condition with a list of variances in said at least one gene indicative of the effectiveness of at least one method of treatment;

b) eliminating a method of treatment from said at least one method of treatment, wherein the presence or absence of at least one of said at least one variance is indicative that said method of treatment will be ineffective or contra-indicated in said patient;

c) selecting an alternative method of treatment effective to treat said disease or condition; and

e. administering said alternative method of treatment to said patient.

104. The method of claim 103, further comprising determining the presence or absence of said at least one variance in cells of said patient.

105. The method of claim 103, wherein said at least one gene comprises a folate transport or metabolism or pyrimidine transport or metabolism gene.

106. The method of claim 103, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase. Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

107. A method for producing a pharmaceutical composition, comprising the steps of:

a) identifying a compound which has differential activity against a disease or condition in patients having at least one variance in a gene;

b) compounding said pharmaceutical composition by combining said compound and a pharmaceutically acceptable carrier or excipient or diluent in manner adapted to be preferentially effective in patients having said at least one variance.

108. A method for producing a pharmaceutical agent, comprising the steps of:

a) identifying a compound which has differential activity against a disease or condition in patients having at least one variance in a gene;

b) synthesizing said compound in an amount sufficient to provide a pharmaceutical effect in a patient suffering from said disease or condition.

109. A method for determining whether a variance in a gene provides variable patient response to a method of treatment for a disease or condition, comprising the steps of:

determining whether the response of a first patient or set of patients suffering from a disease or condition differs from the response of a second patient or set of patients suffering from said disease or condition;

determining whether the presence or absence of at least one variance in at least one folate transport or metabolism gene or pyrimidine transport or metabolism gene differs between said first patient or set of patient and said second patient or set of patients;

wherein correlation of said presence or absence of at least one variance and the response of said patient to said treatment is indicative that said at least one variance provides variable patient response.

110. The method of claim 109, further comprising identifying at least one variance in a said gene.

111. The method of claim 109, wherein a plurality of pairwise comparisons of treatment response and the presence or absence of at least one variance are performed for a plurality of patients.

112. The method of claim 109, wherein said determining whether the presence or absence of at least one variance in at least one gene comprises comparing the response of at least one patient homozygous for said at least one variance with at least one patient homogyzous for the alternative form of said at least one variance.

113. The method of claim 109, wherein said determining whether the presence or absence of said at least one variance in at least one gene comprises comparing the response of at least one patient heterogyzous for said at least one variance with the response of at least one patient homozygous for said at least one variance.

114. The method of claim 109, wherein it is previously known that patient response to said method of treatment is variable.

115. The method of claim 109, wherein said gene is selected from the group consisting of Folate receptor 1(α), Folate receptor (β), Folate receptor (γ), Folate Transporter, Pteroyl-γ-glutamyl carboxypeptidase, Folylpolyglutamate synthetase.

Thymidylate synthase, Formiminotetrahy-drofolate cyclodeaminase, Methenyltetrahy-drofolate synthetase, Methylenetetrahy-drofolate dehydrogenase, Methionine synthetase, Dihydrofolate reductase, Methenyltetrahy-drofolate cyclohy-drolase; formylte-trahydrofolate synthetase; Meth-enyltetrahydrofol-ate dehydrogenase, Glutamate form-iminotransferase, Formyltetrahydrofolate hydrolase, Methylenetetrahydrofolate synthase, Methylenetetrahydrofolate reductase, Serine transhydroxy-methylase, Glycine cleavage system, Protein H, Protein P, Protein T, Protein L, Formyltetrahydrofolate dehydrogenase, Equilibrative nucleoside transporter 1, Equilibrative nucleoside transporters 2, 3, 4 & 5, Uridine phosphorylase, Thymidine phosphorylase, Orotate phosphoribosyl- transferase, Uridine Kinase, Thymidine kinase, Deoxycytidine kinase, Ribonucleoside reductase M1 subunit, Ribonucleoside reductase M2 subunit, Nucleoside diphosphate kinase A subunit, Nucleoside diphosphate kinase B subunit, Uridine mono-phosphate kinase, Deoxycytidylate kinase, Dihydropyrimidine Dehydrogenase, Dihydropyrimidinase, β-ureidopropionase, Cytidine deaminase, dCMP deaminase, and Thymidylate synthase .

116. The method of claim 109, wherein said disease or condition is selected from the group consisting of cancer, proliferative skin diseases, autoimmune diseases, folate deficiency, cardiovascular disease, transplantation, and spina bifida .

117. The method of claim 109, wherein said method of treatment comprises administration of a compound effective to treat said disease or condition.

118. A kit for determination of the presence or absence of at least one sequence variance in a gene identified in any of Tables 2, 6, and 8.

119. The kit of claim 118, wherein said variance is listed in any of Tables 3, 4, 10, and 11.